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EXAMINER	
FORMAN, BETTY J	
ART UNIT	PAPER NUMBER
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/375,248	FERRELL ET AL.	
	Examiner	Art Unit	
	BJ Forman	1634	

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 April 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11,14-21,37 and 38* is/are pending in the application.

4a) Of the above claim(s) *14-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,37 and 38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7*.
4) ☒ Interview Summary (PTO-413) Paper No(s). *21,22*.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Continued Prosecution Application

1. The request filed on 10 April 2002 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/375,248 is acceptable and a CPA has been established. An action on the CPA follows.

2. This action is in response to papers filed 25 April 2002 in Paper No. 20 in which claims 1-7, 14 and 20 were amended and claims 37 and 38 were added. All of the amendments have been thoroughly reviewed and entered. The previous rejections in the Office Action of Paper No. 15 dated 10 October 2001 are withdrawn in view of the amendments. All of the arguments have been thoroughly reviewed but are deemed moot in view of the amendments, withdrawn rejections, and new grounds for rejection.

3. This action is also in response to telephone interviews between Ms. McMillian and the examiner on 17 July 2002 and 19 July 2002. During the first interview, the examiner informed Ms. McMillian that claims previously indicated as allowable are not deemed patentable in view of prior art not discussed by the previous examiner. The examiner provided Ms. McMillian with copies of the prior art document via FAX. During the second interview, Ms. McMillian requested that the examiner restrict the pending claims so that Applicant could elect the method claims while reserving the right to prosecute the product claims in a later application.

4. In view of the newly cited prior art, the examiner's amendments suggested by Examiner Sorbello and approved by Ms. McMillian on 27 June 2002 and 1 July 2002 **have not been entered**.

5. New grounds for rejection are discussed.

6. The restriction is detailed below.

Restrictions

7. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-11, 37 and 38, drawn to a method of assaying for the risk of developing hereditary lymphedema, classified in class 435, subclass 6.

II. Claims 14-17, 20 and 21, drawn to oligonucleotide probes and an array of immobilized oligonucleotide probes, classified in class 536, subclass 24.31 and in class 435, subclass 287.2.

III. Claims 18 and 19, drawn to a kit, classified in class 422, subclass 61.

The inventions are distinct, each from the other because:

Inventions II & III and I are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the products as claimed could be used in a materially different process of using that product i.e. the oligonucleotides of Invention II can be used as templates for peptide synthesis and the kit of Invention III can be used to design sequencing reactions.

8. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

9. During a telephone conversation with Ms. Nebeela McMillian on 19 July 2002 a provisional election was made with traverse to prosecute the invention of Group I, claims 1-11,

37 and 38. Affirmation of this election must be made by applicant in replying to this Office action. Claims 12 withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

10. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

11. Currently claims 1-11, 37 and 38 are under prosecution.

Claim Rejections - 35 USC § 112

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 1-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 1-11 are indefinite in Claim 1 for the recitation "in a manner that reduces ligand-mediated signaling" because "reduces" is a comparative term but it is unclear to what the "signaling" is being compared. It is suggested that Claim 1 be amended to clarify e.g. in line 5, after "allele", insert "when compared to a wild-type allele".

b. Claim 2 is indefinite for the recitation "assaying for a mutation" because it is unclear whether the assaying detects a mutation. It is suggested that the claim be amended to clarify e.g. replace "assaying for" with "identifying".

c. Claims 3 and 4 are each indefinite for the recitation "assaying for a missense mutation in a VEGFR-3 allele at a position corresponding to one of codons...." because it is unclear whether the assaying detects a mutation. The recitation is further in definite because "corresponding' is a non-specific relational phrase. Therefore, the relationship between the mutation and the codons is undefined. It is suggested that Claims 3 and 4 both be amended to clarify.

Claim Rejections - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

15. Claims 1-4, 6-10, 37 and 38 are rejected under 35 U.S.C. 102(a) as being anticipated by Ferrell et al (Human Molecular Genetics 1998, 7(13): 2073-2078).

Regarding Claim 1, Ferrell et al disclose a method of assaying for risk of developing hereditary lymphedema comprising: assaying nucleic acid of a human subject for a mutation altering the encoded amino acid sequence of at least one VEGFR-3 allele in a manner that reduces ligand-mediated signaling of the VEGFR-3 polypeptide and correlating the presence or absence of said mutation to a risk of developing hereditary lymphedema wherein presence of said mutation correlates with an increased risk of and absence of said mutation correlates with no increased risk of developing hereditary lymphedema (page 2076, right column-page 2077, left column).

Regarding Claim 2, Ferrell et al disclose the method wherein the assaying step comprises assaying for a mutation altering a tyrosine domain amino acid sequence of the protein encoded by the VEGFR-3 allele (page 2076, right column, second paragraph). It is noted that Claim 2 is drawn to "assaying for a mutation". Ferrell et al assay for the mutation as claimed. In addition, Ferrell et al identify the mutation.

Regarding Claim 3, Ferrell et al disclose the method wherein the assaying step comprises assaying for a missense mutation in a VEGFR-3 allele at a position corresponding to one of codons 857, 1041, 1044 and 1049 (page 2076, right column, first and second paragraphs). It is noted that Claim 3 is drawn to "assaying for a missense mutation...corresponding to one of codons .....". Ferrell et al assay for corresponding mutations as claimed.

Regarding Claim 4, Ferrell et al disclose the method wherein the assaying step comprises assaying for a missense mutation in a VEGFR-3 allele at a position corresponding to codon 1114 (page 2076, right column, first and second paragraphs). It is noted that Claim 4 is drawn to "assaying for a missense mutation...corresponding to one of codons .....". Ferrell et al assay for corresponding mutations as claimed.

Regarding Claim 6, Ferrell et al disclose the method of Claims 1 and 37 comprising performing a PCR reaction to amplify nucleic acid comprising VEGFR-3 coding region and determining the sequence of the amplified nucleic acid (page 2076, right column, first and second paragraphs).

Regarding Claim 7, Ferrell et al disclose the method of screening for a VEGFR-3 hereditary lymphedema genotype in a human subject comprising: providing a biological sample comprising nucleic acid sequences corresponding to the subject's VEGFR-3 alleles; and determining a VEGFR-3 genotype by analyzing said nucleic acid for the presence of a mutation altering the encoded amino acid sequence of at least one VEGFR-3 allele wherein the presence

of a mutation that reduces signaling of the VEGFR-3 gene identifies hereditary lymphedema genotype (page 2076, right column-page 2077, left column).

Regarding Claim 8, Ferrell et al disclose the method of Claim 7 wherein said biological sample is a cell sample (page 2077, right column, first paragraph).

Regarding Claim 9, Ferrell et al disclose the method of Claim 7 wherein analyzing comprises sequencing a portion of said nucleic acid (page 2077, right column, third paragraph).

Regarding Claim 10, Ferrell et al disclose the method of Claim 7 wherein the nucleic acid is DNA (page 2077, right column, first paragraph).

Regarding Claim 37, Ferrell et al disclose a method of screening a human subject for an increased risk of developing hereditary lymphedema comprising assaying nucleic acid of said subject for a mutation that alters the encoded amino acid sequence of at least one VEGFR-3 allele in a manner that correlates with the risk of developing hereditary lymphedema (page 2076, right column-page 2077, left column).

Regarding Claim 38, Ferrell et al disclose the method wherein said mutation reduces signaling of the VEGFR-3 receptor (Abstract).

Claim Rejections - 35 USC § 103

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

17. Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ferrell et al (Human Molecular Genetics, 1998, 7(13), 2073-2077) in view of Lawrence et al (The American Journal of Human Genetics, October 1998, 63(4), A185, Abstract 1053) and Kimak et al (The American Journal of Human Genetics, October 1998, 63(4), A185, Abstract 180).

Regarding Claim 5, Ferrell et al teach a method of assaying for risk of developing hereditary lymphedema comprising: assaying nucleic acid of a human subject for a mutation altering the encoded amino acid sequence of at least one VEGFR-3 allele in a manner that reduces ligand-mediated signaling of the VEGFR-3 polypeptide and correlating the presence or absence of said mutation to a risk of developing hereditary lymphedema wherein presence of said mutation correlates with an increased risk of and absence of said mutation correlates with no increased risk of developing hereditary lymphedema (page 2076, right column-page 2077, left column) and they teach determining a nucleotide sequence of at least one codon, performing a hybridization assay i.e. microsatellite marker analysis (page 2077, right column) but they do not teach migration assay and restriction digest to determine nucleic acid sequences. However, sequencing, hybridization, migrations and restriction digestion were all well known and routinely practiced in the art at the time the claimed invention was made and Ferrell et al, Lawrence et al and Kimak et al each teach nucleic acid sequence mutations in the VEGFR-3 allele and they teach a correlation between the variations and risk of developing hereditary lymphedema. Additionally, Lawrence et al teach at least one of the known VEFFR-3 mutations is identified by restriction digestion. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply routinely practiced techniques to detect the mutations disclosed by Ferrell et al, Lawrence et al and Kimak et al and to perform sequencing, hybridization, migration assay and restriction digestion to thereby accurately and completely analyze and compare a sample sequences for obvious benefits of accurate diagnosis of a clinically important mutations.

18. Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ferrell et al (Human Molecular Genetics, 1998, 7(13), 2073-2077).

Regarding Claim 11, Ferrell et al teach a method of assaying for risk of developing hereditary lymphedema comprising: assaying nucleic acid of a human subject for a mutation altering the encoded amino acid sequence of at least one VEGFR-3 allele in a manner that reduces ligand-mediated signaling of the VEGFR-3 polypeptide and correlating the presence or absence of said mutation to a risk of developing hereditary lymphedema wherein presence of said mutation correlates with an increased risk of and absence of said mutation correlates with no increased risk of developing hereditary lymphedema (page 2076, right column-page 2077, left column) wherein the nucleic acid is DNA (page 2077, right column, first paragraph) but they do not teach the nucleic acid is RNA. However, RNA analysis for the purpose of analyzing expressed sequences was well known and routinely practiced in the art using methods similar and/or equal to those for analyzing DNA. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the DNA of Ferrell et al and to analyze RNA based on similar analytical methods for the obvious benefits of analyzing expressed i.e. encoding sequences.

Conclusion

19. No claim is allowed.

20. The Examiner and Art Unit for this application have changed. Please address future correspondence to BJ Forman, Art Unit: 1634.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:30 TO 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

BJ Forman, Ph.D.
Patent Examiner
Art Unit: 1634
July 22, 2002